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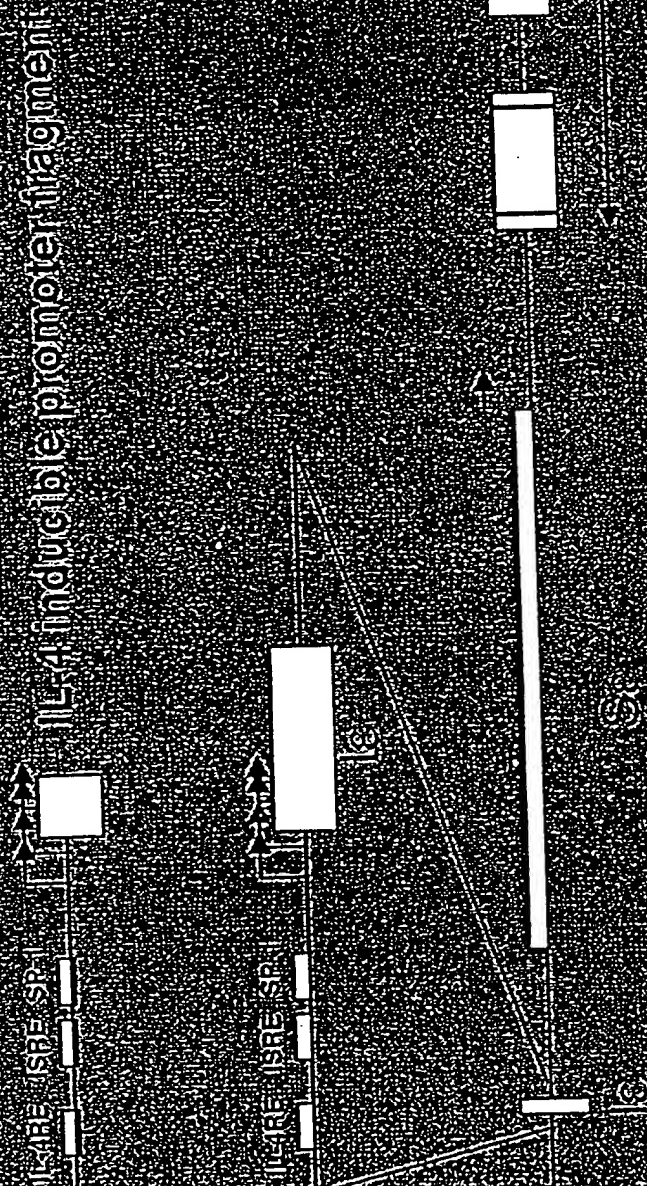
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CTCGAGGACAGTGACCTGGGAGTGAGTACAAGGTGAGGCCACCACTCAGGGT  
GCCAGCTCCAAGCGGGTCACAGGACGAGGGCTGCGGCCATCAGGAGGCCCT  
GCACACACATCTGGGACACGCGCCCCGAGGGCCAGTTCACCTCAGTGCGCCT  
CATTCTCTGCACAAAAGCGCCCCATCCTTTCTTACAAGGCTTTCTGTGGAAG  
CAGAGGCGTCGATGCCCAGTACCCTCTCCCTTTCCAGGCAACGGGACCCCAA  
GTTTGCTGACTGGGACCACCAAGCCACGCATGCGTCAAGAGTGAGAGTCCGG  
GACCTAGGCAGGGGCCCTGGGGTTGGGCCTGAGAGAGAAGAGAACCTCCCCC  
AGCACTCGGTGTGCATCGGTAGTGAAGGAGCCTCACCTGACCCCCGCTGTTGC  
TCAATCGACTTCCCAAGAACAGAGAGAAAAGGGAACCTCCAGGGCGGCCCGG  
GCCTCCTGGGGGTTCCCACCCCATTTTTAGCTGAAAGCACTGAGGCAGAGCTC  
CCCCTACCCAGGCTCCACTGCCCGGCACAGAAATAACAACCACGGTTACTGAT  
CATCTGGGAGCTGTCCAGGAATTC

# Germpline & Locus



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**FIGURE 1B**

# Low energy DNA folding of the $S_{\epsilon}$ region

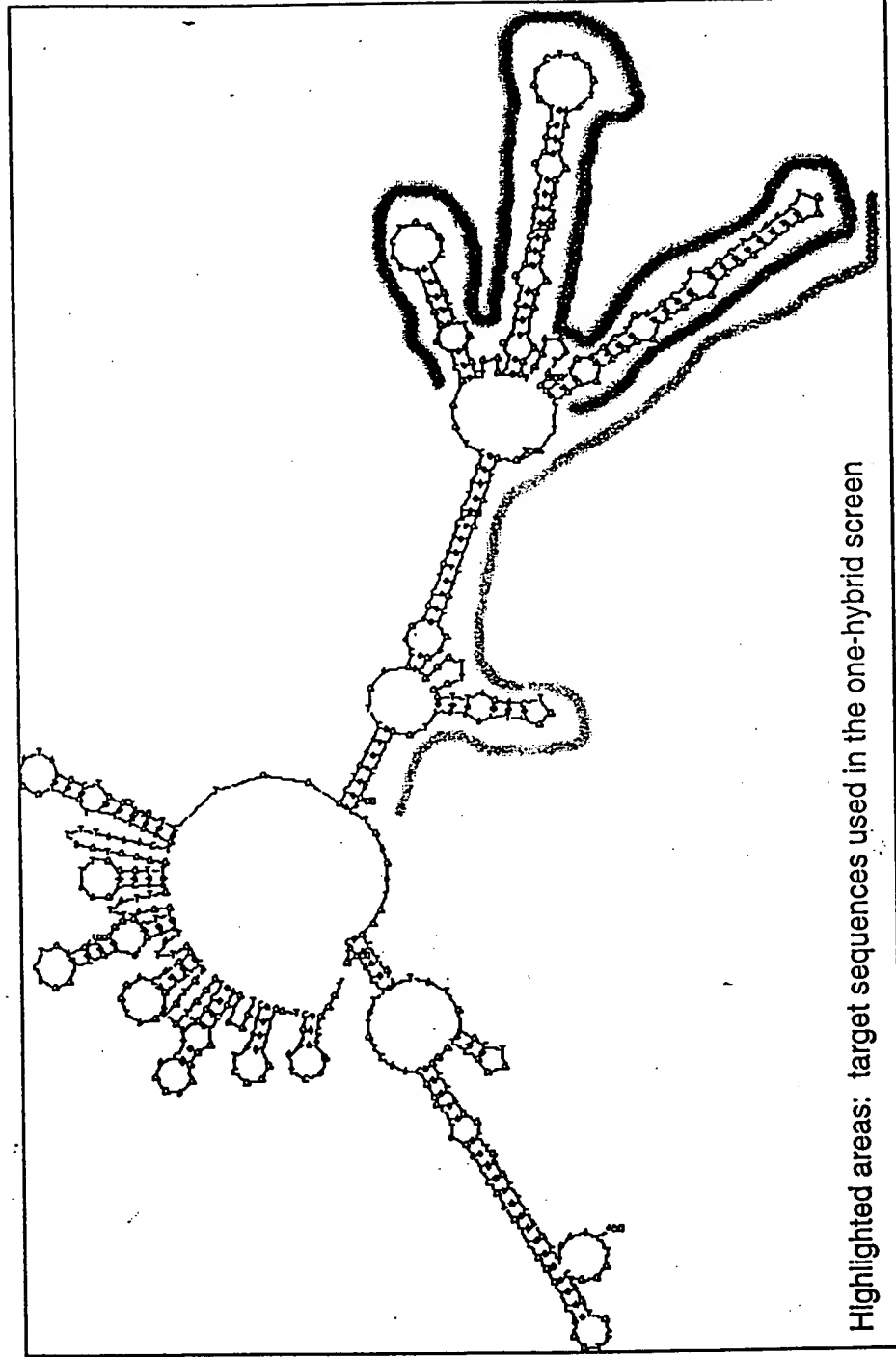


FIG 2A

## FIGURE 2B

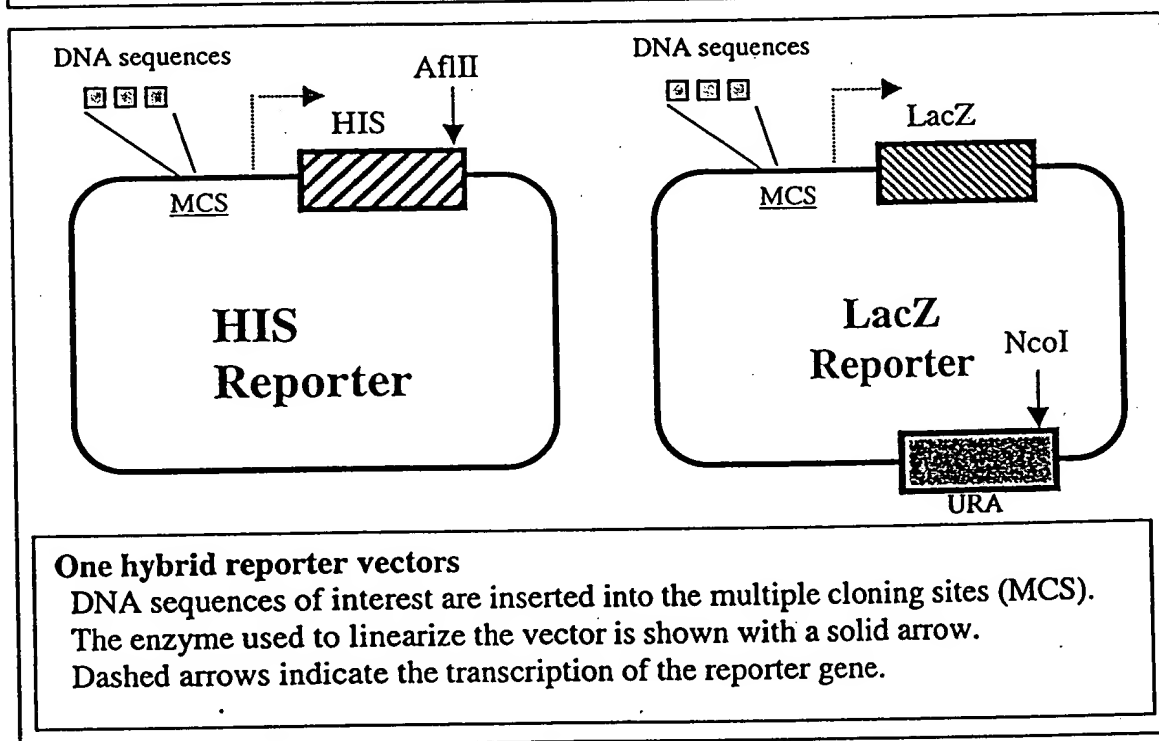
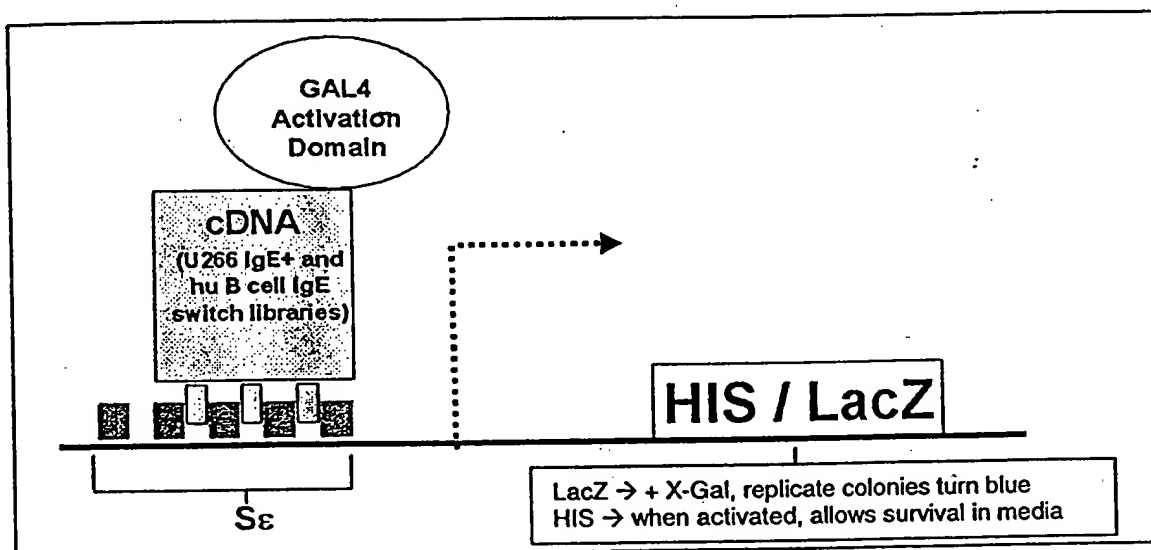
1 GCTGGGCTAA ACTGGGCTAG CCTGAGCTGG GCTGAACTGG GCTGCTGGGC  
51 TGGACTGGGT AAGCTGGGCT GAGCTGGGTT GGGTGGAAAT GGGCTGAGCT  
101 GAGCTAGGCT AAACCTGGGTT TGGCTGGGCT GGGCTGGGCT GGG

## FIGURE 2C

1 GGTTTGGCTG GGCTGGGCTG GGCTGGGCTG GGTTTCAGCTG AGCGGGTTGG  
51 GTTAGACTGG GTCAAACCTGG TTCAGC

FIG 3

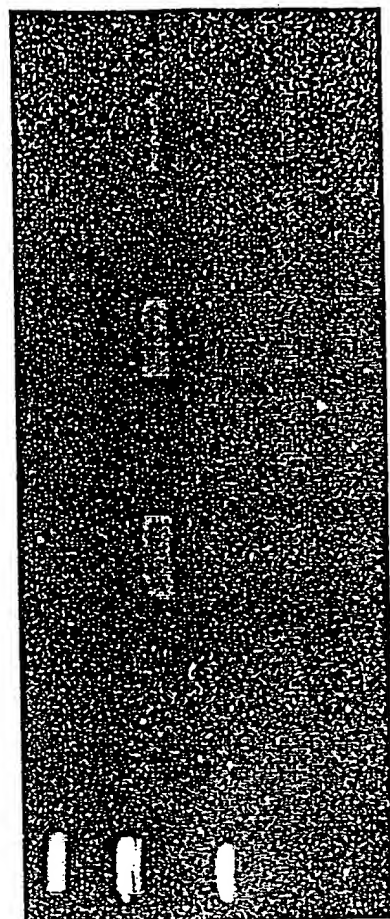
# Appendix F Yeast One-Hybrid Screening



# IL-4 Induction of Germline $\epsilon$ mRNA in the IgM+ B cell lines: CA-46, MC-116 and DND39

Cells were incubated for 48 hrs in 300 U/ml of h-IL-4. RT-PCR was performed using primers specific for the germline  $\epsilon$  exon and the 5'-end of the  $\epsilon$  CH1 exon (predicted size ~ 200 bp).

DND39 + IL-4  
DND39 - IL-4  
MC-116 + IL-4  
MC-116 - IL-4  
CA-46 + IL-4  
CA-46 - IL-4  
Neg cont.



# Approaches to generate germline $\epsilon$ promoter knock-in reporter cell lines

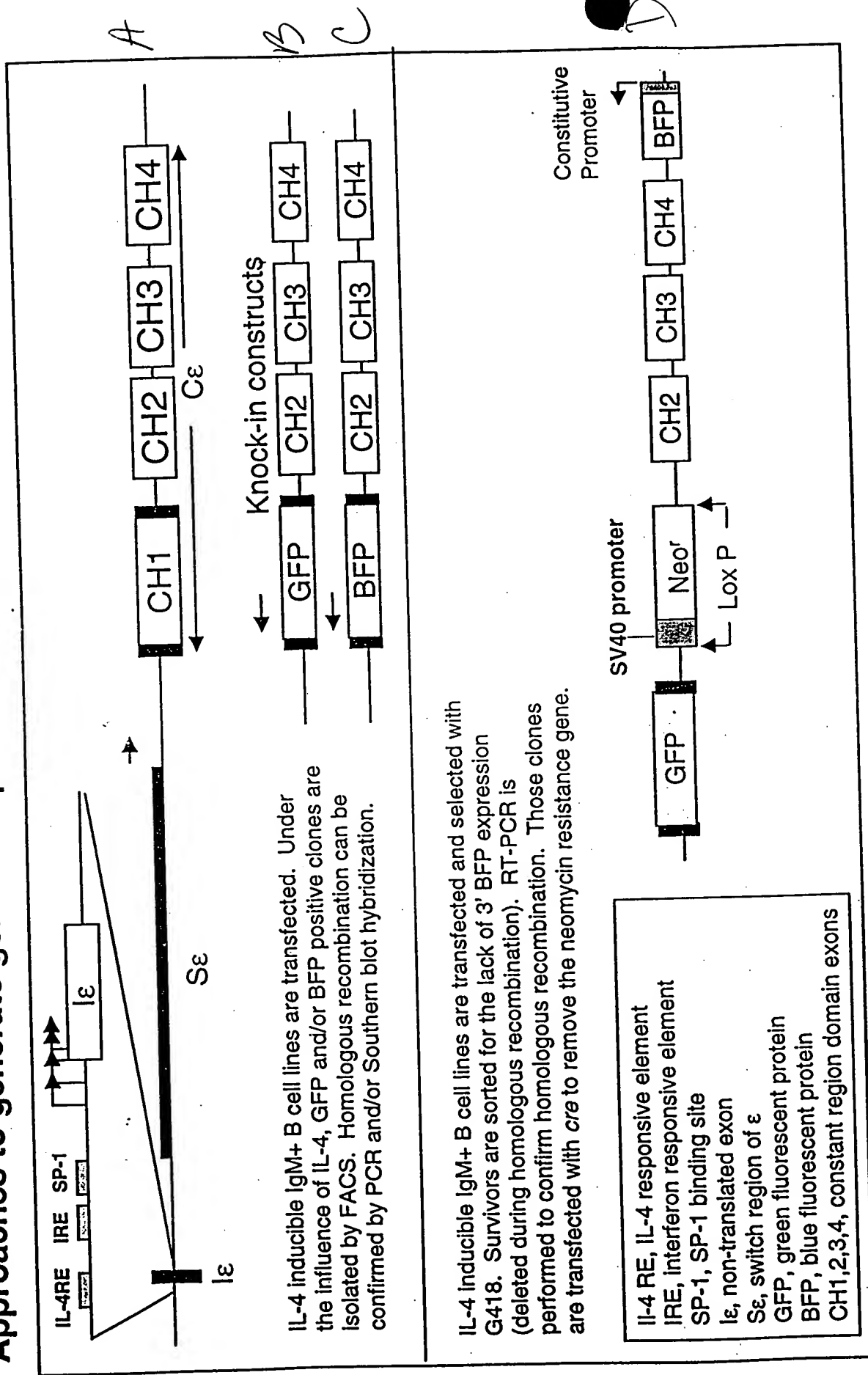
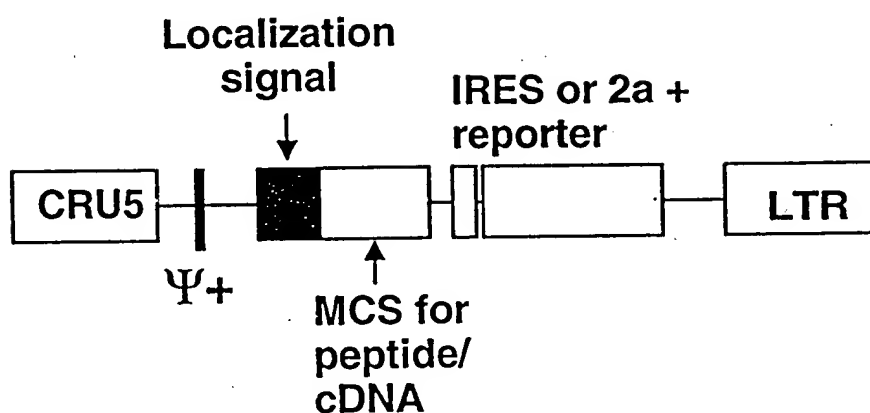


FIG 6

## Appendix I

### Rigel Base Vector



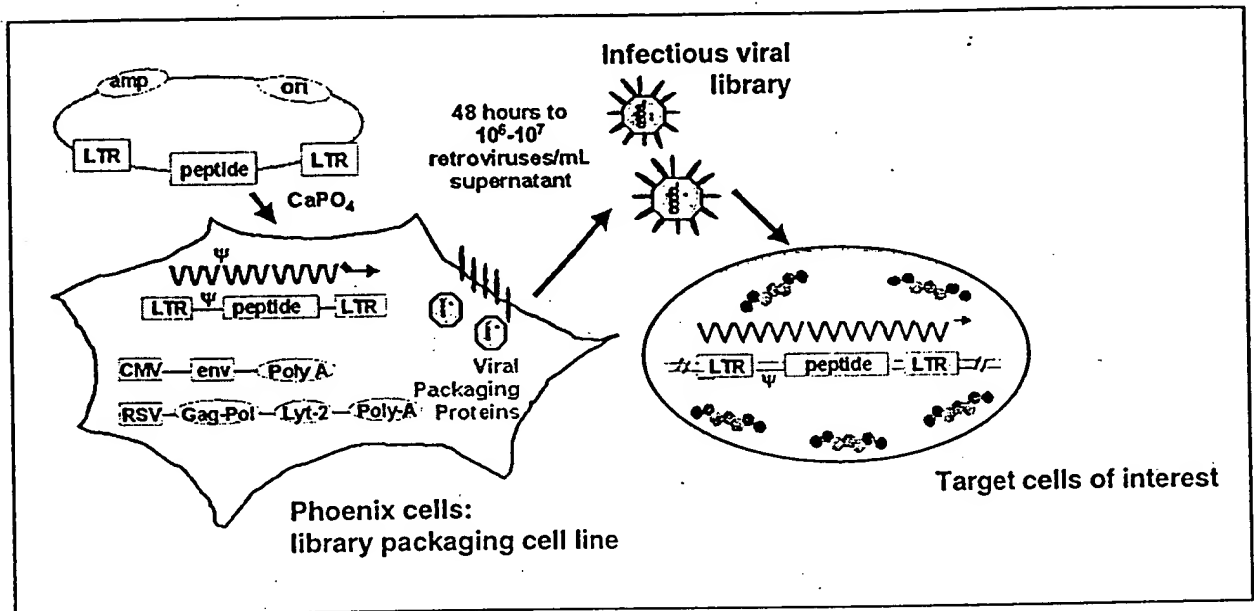
All components are cassetted for flexibility

CRU5, modified LTR  
LTR, long terminal repeat  
 $\Psi+$ , packaging signal  
Localization signal: nuclear, cell membrane, granular  
MCS, multiple cloning site  
IRES, internal ribosome entry site  
2a, self-cleaving peptide

FIG - 7

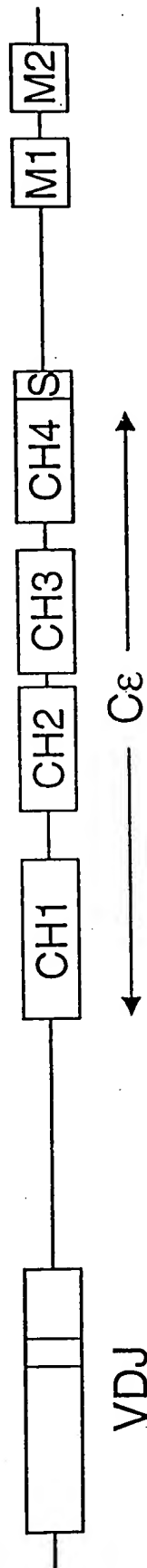
## Appendix H

### Protocol for Transfection of Phoenix Cells and Infection of Nonadherent Target Cells

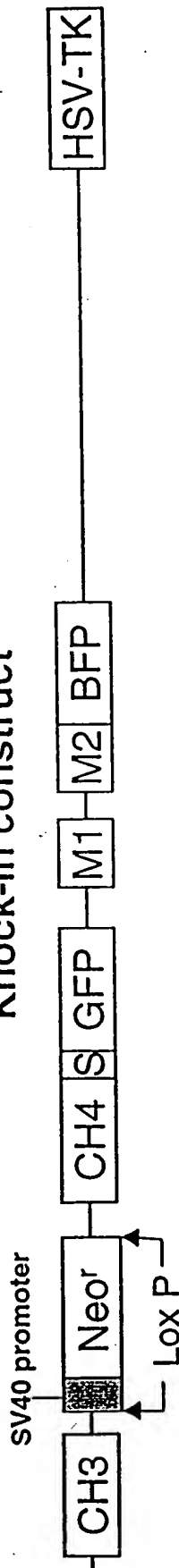


# $\epsilon$ heavy chain GFP/BFP knock-in cell line

## U266 $\epsilon$ heavy chain



## Knock-in construct

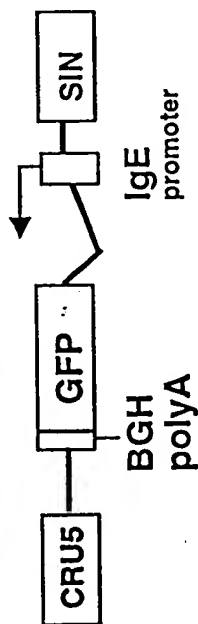


U266 cells are transfected and selected with G418. Survivors are treated with ganciclovir (HSV-TK deleted during homologous recombination). RT-PCR is performed to confirm homologous recombination. Those clones are transfected with *cre* to remove the SV40 neomycin resistance gene.

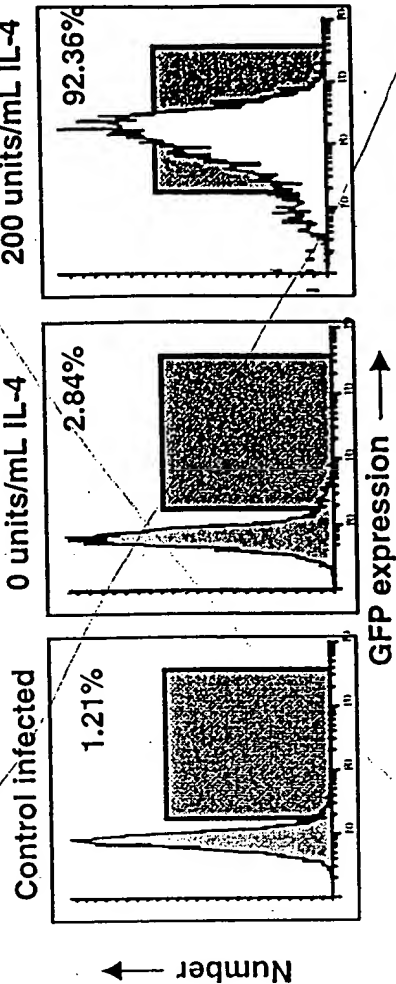
S, secretory exon  
GFP, green fluorescent protein  
BFP, blue fluorescent protein  
Neo<sup>r</sup>, neomycin resistance gene  
VDJ, V region exon  
CH1,2,3,4, constant region domain exons  
M1, M2, membrane exons  
HSV-TK, Herpes Simplex virus-Thymidine Kinase

# IL-4 Inducible ε Promoter Reporter Cell Line

## Report r construct

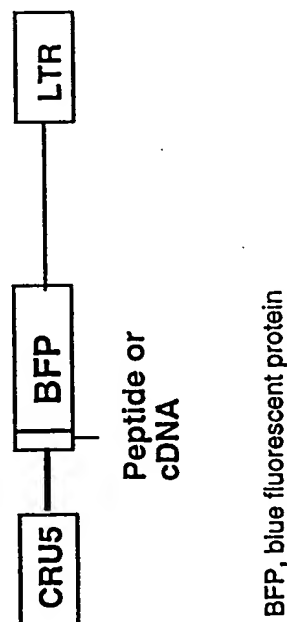


## IL-4 induced reporter

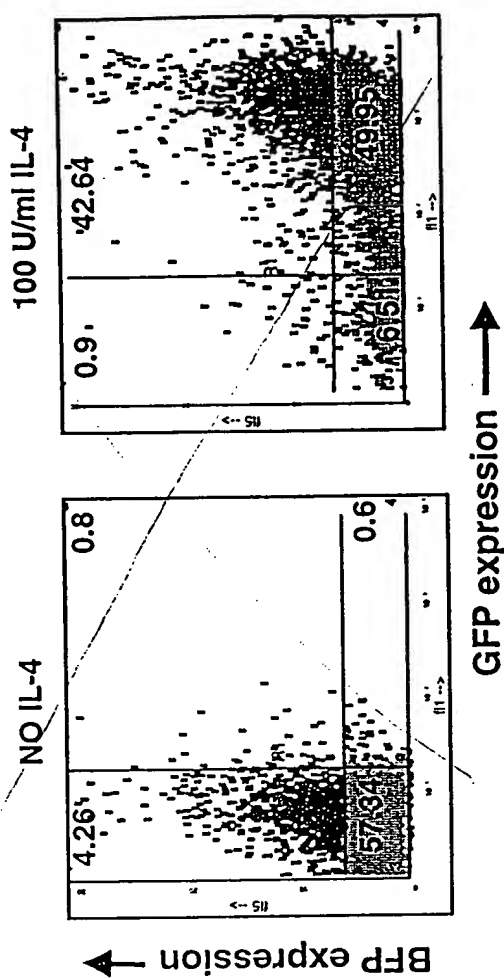


## Reporter Line Infected with BFP Construct

### Library construct

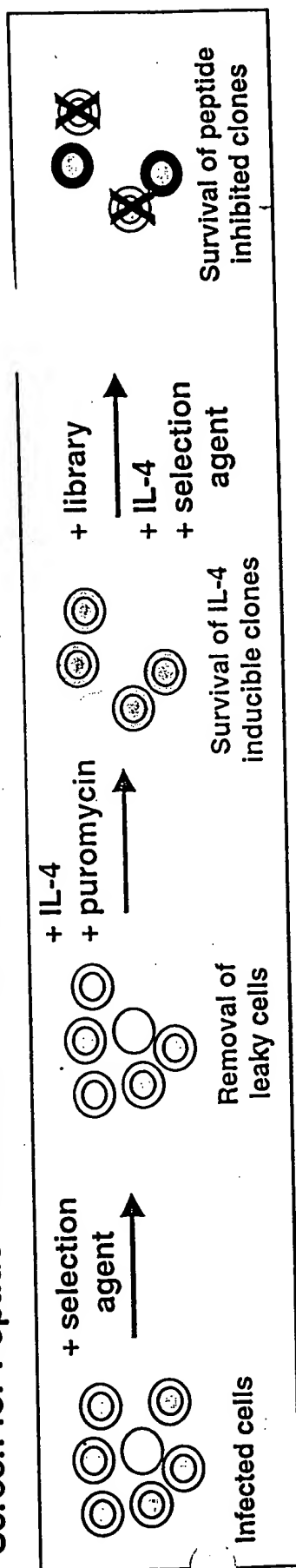


### FACS profile of cells with both reporter and peptide library

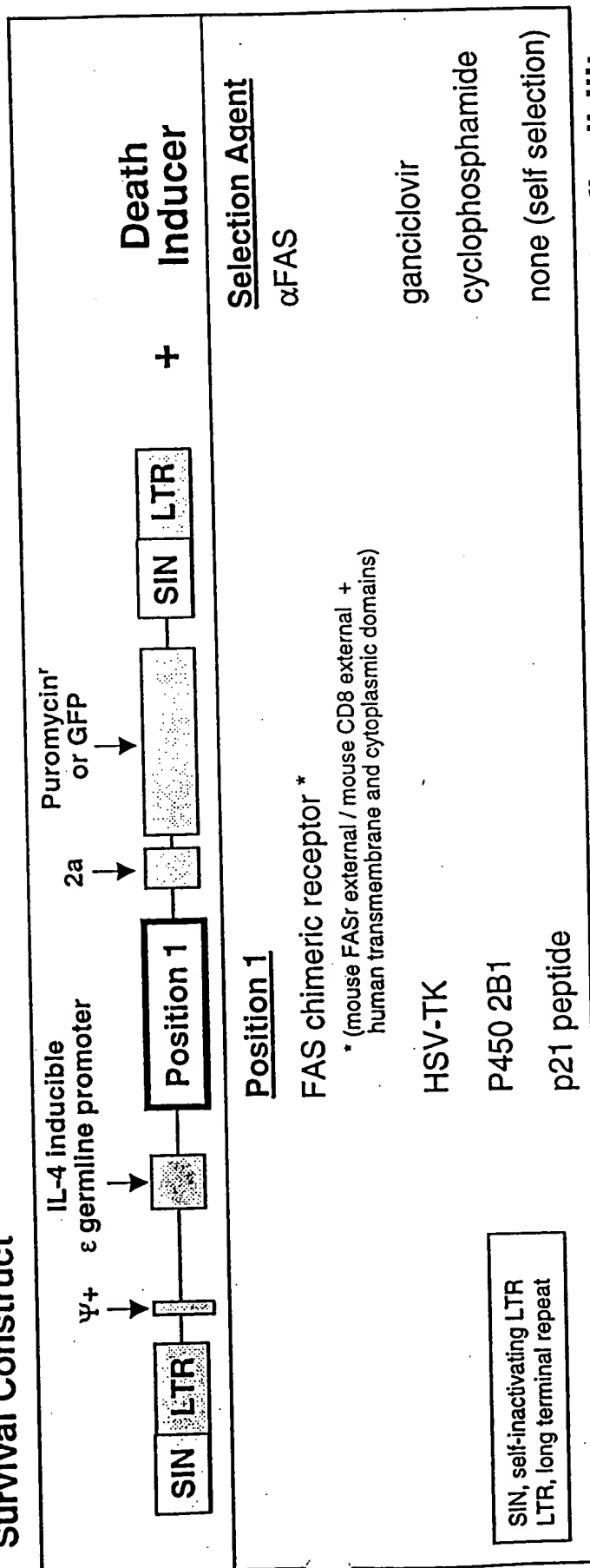


## Appendix C

# Screen for Peptide Inhibitors of the Germline $\epsilon$ Promoter



## Survival Construct



## All components are cassetted for flexibility

## Appendix D

# FIGURE 11A-1

1-845 CMV promoter/R/U5 5' LTR  
 1322 GAG ATG-ATC mutation  
 850-2100 extended  $\psi$  region  
 2146-2173 two Bstx1 peptide cloning sites  
 2205-2723 ECMV IRES (cloned as EcoR1/MscI fragment from  
 pCITE-4a [Novagen])  
 2746-3465 GFP coding region  
 3522-4115 3' LTR  
 4122-6210 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATCC  
 CAAACTCAAATATATAAAGCATTGACTTGTCTATGCCCTAGTTATTAATAGTAATCAA  
 TTACGGGGTTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAA  
 ATGGCCCGCTGGCTGACCGCCCAACGACCCCGCCCATTGACGTCAATAATGACGTATG  
 TTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGT  
 AAAGTGGCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG  
 TCAATGACGGTAAATGGCCCGCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTC  
 CTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGTATGCGGTTTTGGC  
 AGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCTCAAGTCTCCACCCCA  
 TTGACGTCAATGGGAGTTTGTGTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA  
 ACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGAGGTCTATATAA  
 GCAGAGCTCAATAAAAGAGCCCAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACT  
 GAGTCGCCCCGGGTACCCGTGTATCCAATAAACCCCTCTTGCAAGTTGCATCCGACTTGTGGT  
 CTCGTGTTCCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTT  
 CATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCAGGGACCACCGACCCACCACCG  
 GGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCTAGTGTCTATGACTGA  
 TTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGTATCTGGCGGACCCGTGG  
 TGGAAGTACGAGTTCGGAACACCCCGCCCAACCCCTGGGAGACGTCCCAGGGACTTCGG  
 GGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAATCCCGATCGTTTTTGGACTCTTTGGTG  
 CACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGACGAGAACCTAAAACAGTTCC  
 CGCCTCCGTCTGAATTTTGTGCTTTTCGGTTTTGGGACCGAAGCCGCGCGCGCTCTGTCT  
 GCTGCAGCATCGTTCTGTGTTGTCTCTGACTGTGTTTCTGTATTTGTCTGAAAATA  
 TCGGCCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTGACCTTAGGTCACTGGAAAGATG  
 TCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTTACCTTCT  
 GCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGCCGCGAGACGGCACCTTTAACCGAG  
 ACCTCATCACCCAGGTTAAGATCAAGGTCTTTTACCTGGCCCCGCATGGACACCCAGACC  
 AGGTCCCCCTACATCGTGACCTGGGAAGCCTTGCTTTTGACCCCCCTCCCTGGGTCAAGC  
 CCTTTGTACACCTAAGCCTCCGCCTCCTCTTCCCTCATCCGCCCCGTCTCTCCCCCTTG  
 AACCTCCTCGTTTCGACCCCGCCTCGATCCTCCCTTTATCCAGCCCTCACTCCTTCTCTAG  
 GCGCCCCCATATGGCCATATGAGATCTTATATGGGGCACCCCGCCCCCTTGTAACCTTCC  
 CTGACCCTGACATGACAAGAGTTACTAACAGCCCTCTCTCCAAGCTCACTTACAGGCTC  
 TCTACTTAGTCCAGCAGCAAGTCTTGAGACCTCTGGCGGCAGCCTACCAAGAACAAGTG  
 ACCGACCGGTGGTACCTCACCTTACCAGTTCGGCGACACAGTGTGGGTCCGCGGACACC  
 AGACTAAGAACCTAGAACCTCGCTGGAAAGACCTTACACAGTCTTGCTGACCACCCCA  
 CCGCCCTCAAAGTAGACGGCATCGCGCTTGATACACGCGCCACGTGAAGGTGCGCGA  
 CCGCGGGGTGGACCATCCTCTAGACTGCCGGATCTCGAGGGATCCACCACCATGGACCC  
 CCATTAAATTGGAATTCCTGCAGCCCGGGGATCCACTAGTTCTAGAGCGAATTAATTCC

FIGURE 11A-2

GGTTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTG  
TCTTCTTGACGAGCATTCCCTAGGGGTCTTTCCCTCTCGCCAAAGGAATGCAAGGTCTGT  
TGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGACAAACAACGTCTGTAG  
CGACCCTTTGCAGGCAGCGGAACCCCCACCTGGCGACAGGTGCCTCTGCGGCCAAAAGC  
CACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCACGTGCCACGTTGTGAGTTGGA  
TAGTTGTGGAAGAGTCAAATGGCTCTCCTCAAGCGTATTCACAAGGGGCTGAAGGATG  
CCCAGAAGGTACCCCATTTGTATGGGATCTGATCTGGGGCCTCGGTGCACATGCTTTACAT  
GTGTTTAGTCGAGGTTAAAAACGTCTAGGCCCCCGAACCACGGGGACGTGGTTTTCTCT  
TTGAAAAACACGATGATAATATGGGGGATCCACCGGTGCGCCACCATGGTGAGCAAGGGCG  
AGGAGCTGTTACCGGGGTGGTGCCCATCCTGGTTCGAGCTGGACGGCGACGTAAACGGCC  
ACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGA  
AGTTCATCTGCACCACCGGCAAGCTGCCCCGTGCCCTGGCCACCCCTCGTGACCACCCTGA  
CCTACGGCGTGCAGTGCTTCAGCCGCTACCCCGACCACATGAAGCAGCAGCACTTCTTCA  
AGTCCGCCATGCCCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCA  
ACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGC  
TGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAAC  
ACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAAC  
TCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGA  
ACACCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCCTACCTGAGCACCCAGT  
CCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCTCTGCTGGAGTTCTGTGA  
CCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAAAGCGGCCGCTCGACGA  
TAAAAATAAAGATTTTATTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCACCTGTA  
GGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGAAGGCATGGAAAAATACATAACTGA  
GAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACA  
GGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTG  
AATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAA  
CAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTC  
CAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTTCG  
CTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCC  
TCACTCGGGGCGCCAGTCCCTCCGATTGACTGAGTCGCCCCGGGTACCCGTGTATCCAATAA  
ACCTCTTTGACGTTGCATCCGACTTGTGGTCTCGCTGTTCCCTTGGGAGGGTCTCCTCTGA  
GTGATTGACTACCCGTCAGCGGGGGTCTTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGG  
GAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCACATGCAGCATGTAT  
CAAAATTAATTTGGTTTTTTTTTCTTAAGTATTTACATTAATGGCCATAGTTGCATTAAT  
GAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCATTTGGCGCTCTTCCGCTTCTCTCGCT  
CACTGACTCGCTGCGCTCGGTCTGTTTCGGCTGCGGCGAGCGGTATCAGCTCAAAAGGC  
GGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGG  
CCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCG  
CCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGG  
ACTATAAAGATAACAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGAC  
CCTGCCGCTTACCGGATACCTGTCCGCTTTCTCCCTTCGGGAAGCGTGCGCTTTCTCA  
TAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCTGCTCCAGCTGGGCTGTGT  
GCACGAACCCCCGTTTACGCCCCGACCGCTGCGCCTTATCCGGTAACATCGTCTTGAGTC  
CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG  
AGCGAGGTATGTAGGCGGTGCTACAGAGTCTTGAAGTGGTGGCCTAACTACGGCTACAC  
TAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGT  
TGGTAGCTCTTGATCCGGCAAACAACACCGCTGGTAGCGGTGGTTTTTTTGTGTTGCAA  
GCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGG  
GTCTGACGCTCAGTGGAACGAAACTCACGTTAAGGGATTTTGGTTCATGAGATTATCAAA  
AAGGATCTTCACCTAGATCCTTTTAAATTAATAAAGTAAAGTTTGGCGAAATCAATCTAAAG  
TATATATGAGTAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTC  
AGCGATCTGTCTATTTTCGTTTCATCCATAGTTGCCTGACTCCCCGTGCTGTAGATAACTAC  
GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC  
ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGG

FIGURE 11A-3

TCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAG  
TAGTTCGCCAGTTAATAGTTTGC GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTC  
ACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTCCCAACGATCAAGGCGAGTTAC  
ATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAG  
AAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTAC  
TGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTG  
AGAATAGTGATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAATACCGC  
GCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAAC  
CTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTG  
ATCTTCAGCATCTTTTACTTTTACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAA  
TGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTT  
TCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATG  
TATTTAGAAAAATAAACAAATAGGGGTTCGCGCACATTTT

# FIGURE 11B-1

1-845 CMVpormoter/R/U5 5' LTR  
 1322 GAG ATG-ATC mutation  
 850-2100 extended □ region  
 2151-2865 GFP coding region  
 2866-2894 GGS SGGG linker  
 2895-2952 FMDV 2a cleavage sequence  
 2953-3004 Bstx1/Bstx1/Hind3/Hpa1/Sal1/Not1 polylinker  
 3052-3645 3' LTR  
 3652-5715 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGCTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTQCTAATACATC  
 CCAAAC TCAAATATATAAAGCATTTGACTTGTCTATGCCCTAGTTATTAATAGTAATC  
 AATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGG  
 TAAATGGCCCCGCTGGCTGACCGCCCAACGACCCCCGCCCATTTGACGTCAATAATGACG  
 TATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTT  
 ACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTA  
 TTGACGTCAATGACGGTAAATGGCCCCGCTGGCATTATGCCCAGTACATGACCTTATGG  
 GACTTTCCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG  
 GTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGA CTACG GGGATTTC CAAGTC 53  
 5' 10' TCCACCCCATTTGACGTCAATGGGAGTTTGT TTTGGCACCAAAATCAACGGGACTTTCCA  
 AAATGTCGTAACA ACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGA  
 GGTCTATATAAGCAGAGCTCAATAAAAGAGCCCAACCCCTCACTCGGGGCGCCAGTC  
 CTCCGATTGACTGAGTCGCCCCGGGTACCCGTGTATCCAATAAACCCCTCTTGCA GTTGCA  
 TCCGACTTGTGGTCTCGCTGTTCCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGT  
 CAGCGGGGGTCTTTTCA TTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACC  
 ACCGACCCACCACGGGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTC  
 TAGTGTCTATGACTGATTTTATGCGCCTGCGTCCGGTACTAGTTAGCTAACTAGCTCTGT  
 ATCTGGCGGACCCGTGGTGGA ACTGACGAGTTCGGAACACCCGGCCGCAACCCCTGGGAG 5' 53  
 1062 18

FIGURE 11B-2

ACGTCCCAGGGACTTCGGGGGCGGTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGAT  
CGTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGA  
CGAGAACCTAAAACAGTTCCTCGCCTCCGTCTGAATTTTGGCTTTCGGTTTGGGACCGAA  
GCCGCGCCGCGCGTCTTGTCTGCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTG  
TTTCTGTATTTGTCTGAAAATATCGGCCCCGGGCCAGACTGTTACCACTCCCTTAAGTTT  
GACCTTAGGTCACTGGAAAGATGTGAGCGGATCGCTCACAACCAGTCCGTTAGATGTCA  
AGAAGAGACGTTGGGTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGG  
CCGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTAAAGATCAAGGTCTTTTC  
ACCTGGCCCCGCATGGACACCCAGACCAGGTCCCCCTACATCGTGACCTGGGAAGCCTTGG  
CTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCCTAAGCCTCCGCTCCCTCTT  
CCTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTGACCCCGCCTCGATCCTC  
CCTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTAT 30-1770  
ATGGGGCACCCCCGCCCCCTTGTAAACTTCCCTGACCCTGACATGACAAGAGTTACTAAC  
AGCCCCCTCTCTCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAG  
ACCTCTGGCGGCAGCCTACCAAGAACAACTGGACCGACCGGTGGTACCTCACCTTACC  
GAGTCGGCGACACAGTGTGGGTCCGCGGACACCAGACTAAGAACCCTAGAACCTCGCTGG  
5 AAAGGACCTTACACAGTCTCTGCTGACCACCCCCACCGCCCTCAAAGTAGACGGCATCGC 2006  
AGCTTGATACACGCCGCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTA  
GACTGCCGGATCTCGAGGGATCCACCATGGTGAGCAAGGGCGAGGAGCTGTTACCGGG  
GTGGTGCCCATCCTGGTTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTG  
CGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCA  
CCGGCAAGCTGCCCGTGCCCTGGCCACCTCGTGACCACCTGACCTACGGCGTGCAG 40-2360  
TGCTTCAGCCGCTACCCCGACCATGAAGCAGCAGACTTCTTCAAGTCCGCCATGCC  
CGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCC  
GCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATC  
GACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACCTACAACAGCCA  
CAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAAGTTCAGATCC  
GCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAACACCCCC  
ATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGTCCGCCCT  
GAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCG  
CCGGGATCACTCTCGGCATGGACGAGCTGTACAAGGAATTCCGAGGTGGCAGCGGTGGC  
GGTCAGCTGTTGAATTTTGACCTTCTTAACTTGCGGGAGACGTGAGTCCAACCTGG 50-2450  
GCCCACCACCACCATGGAAGCTTCCATTAAATTGGTTAACGTCGACGCGGCCGCTCGAC  
GATAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCACCT  
GTAGGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAA  
CTGAGAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCC  
AAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAA  
CAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGG  
CCAAGAACAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCA  
GATGTTTCCAGGGTGGCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCA  
ATCAGTTCGCTTCTCGCTTCTGTTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGC  
CCACAACCCCTCACTCGGGGCGCCAGTCTCCGATTGACTGAGTCGCCCCGGGTACCCGT  
GTATCCAATAAACCCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAG  
GGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTTTCAATTTCCGACTTGTGGT  
CTCGCTGCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCA  
CATGCAGCATGTATCAAAATTAATTTGGTTTTTTTTCTTAAGTATTTACATTAAATGGC  
CATAGTTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTTCGTATTGGCGCT

100

T<sub>S</sub> - 32

5.7.13

# FIGURE 11C-1

1-845 CMVpormoter/R/U5 5' LTR  
1322 GAG ATG-ATC mutation  
850-2100 extended  $\square$  region  
2146-2173 two Bstx1 peptide cloning sites  
2173-2214 EoR1/Apa1/Hpa1/Not1 polylinker  
2262-2855 3' LTR  
2855-4901 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCCTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATCCCAAACTCAAAT-  
ATATAAAGCATTGACTTGTCTATGCCCTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAG  
CCATATATGGAGTTCGCGTTACATAACTTACGGTAAATGGCCCGCTGGCTGACCGCCCAACGACCCCG  
CCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGG  
TGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATT  
GACGTCAATGACGGTAAATGGCCCGCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCTACTTGT  
GCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAATGGGCGTG  
GATAGCGGTTTGACTCACGGGGATTTCGAAGTCTCCACCCCATTTGACGTCAATGGGAGTTTGTTTGGCAC  
CAAATCAACGGGACTTTCCAAATGTCTGAACAACCTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGT  
ACGGTGGGAGGTCTATATAAGCAGAGCTCAATAAAAGAGCCCAACCCCTCACTCGGGGCGCCAGTCCCTC  
CGATTGACTGAGTCGCGCGGTACCCGTGTATCCAATAAACCCCTCTGTCAGTTGCATCCGACTTGTGGTCT  
CGCTGTTCTTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGCTTTTCATTTGGGGGCTC  
GTCCGGGATCGGGAGACCCCTGCCAGGGACCCGACCCACCACCGGGAGGTAAGCTGGCCAGCAACTTA- 1) 923  
TCTGTGTCTGTCCGATTGTCTAGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACT  
AGCTCTGTATCTGGCGGACCCGTGGTGAACTGACGAGTTTCGGAACACCCGGCCGCAACCCCTGGGAGACGT  
CCCAGGGACTTCGGGGGCGGTTTTTGTGGCCGACCTGAGTCCAAAAATCCCGATCGTTTGGACTCTTTG  
GTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGACGAGAACCCTAAAACAGTTCCCGCCTCCG  
TCTGAATTTTGTCTTTTCGGTTTGGGACCGAAGCCGCGCGCGCTCTGTCTGCTGCAGCATCGTTCTGTG  
TTGTCTCTGTCTGACTGTGTTTCTGTATTTGTCTGAAAATATCGGCCCGGGCCAGACTGTACCCTCCCT  
TAAGTTTGACCTTAGGTCACTGGAAGATGTGCGAGCGGATCGTCAACACCGTCCGTAGATGTCAAGAAG- 20 - 1420  
AGACGTTGGGTACCTTCTGCTCTGCGAATGGCCAACTTTAACGTCGGATGGCCGCGAGACGGCACCTT  
TAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTTCACCTGGCCCGCATGGACACCCAGACCAGG  
TCCCTACATCGTGACCTGGGAAGCCTTGGCTTTTGAACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCT  
AAGCCTCCGCTCCTCTTCTCCATCCGCCCCGCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCG  
ATCCTCCCTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTATATGGGG- 15 1775  
CACCCCCGCCCCCTGTAACTTCCCTGACCTGACATGACAAGAGTTACTAACAGCCCTCTCTCCAAGCT  
CACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAAC  
GGACCGACCGGTGGTACCTCACCTTACCGAGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGA- 28 - 1448  
ACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCTGTGCTGACACCCCGCCGCTCAAAGTAGACGGC  
ATCGCAGCTTGGATACACGCGCCGACGTAAGGCTGCCGACCCCGGGGTGGACCATCCTCTAGACTGCC- 30 - 2130  
GGATCTCGAGGGATCCACCACCATGGACCCCCATTAAATTGGAATTCGGGGGCCAAGCTTTGTAAACGTG  
ACGCGCGCGCGCTCGACGATAAAATAAAAGATTTTATTTAGTCTCCAGAAAAGGGGGGAATGAAAGACCC  
CACCTGTAGGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGAGAA  
TAGAGAAGTTTCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACAGGATATCTGTGGTA  
AGCAGTTCTGCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGT  
GGTAAGCAGTTCTGCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGT  
TTCTAGAGAACCATCAGATGTTTCCAGGGTGGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTA  
ACCAATCAGTTCTGCTTCTGCTTCTGTTGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCAAC  
CCTCACTCGGGGCGCCAGTCTCCGATTGACTGAGTCGCGCGGTACCCGTGTATCCAATAAACCCCTTTG

FIGURE 11C-2

CAGTTGCATCCGACTTGTGGTCTCGCTGTTCCCTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGC  
GGGGGTCTTTTCAATTTCCGACTTGTGGTCTCGCTGCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGT  
CAGCGGGGGTCTTCACATGCAGCATGTATCAAAATTAATTTGGTTTTTTTTTCTTAAGTATTTACATTAAAT  
GGCCATAGTTGCATTAATGAATCGGCCAACGCGCGGGAGAGGCGGTTTGCGTATTGGCGCTCTTCCGCTT  
CCTCGCTCACTGACTCGCTGCGCTCGGTTCGGCTGCGCGAGCGGTATCAGCTCACTCAAAGGCGGTA  
ATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAGGCCAGCAAAGGCCAG  
GAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAATC  
GACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCC  
CTCGTGCGCTCTCTGTTCCGACCTGCGCTTACCGGATACCTGTCCGCTTTCTCCCTTCGGGAAGCGT  
GGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCCGGTGTAGGTCTCGCTCCAAGCTGGGCTGTG  
TGCACGAACCCCCGTTTACGCCCCGACCGCTGCGCTTATCCGGTAACATATCGTCTTGAGTCCAACCCGTA  
AGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGC  
TACAGAGTTCTTGAAGTGGTGGCTTAACACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGC  
TGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGT  
GGTTTTTTTGTGTTGCAAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTC  
TACGGGGTCTGACGCTCAGTGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGA  
TCTTACCTAGATCCTTTTAAATTAATAATGAAGTTTGGCGAAATCAATCTAAAGTATATATGAGTAACT  
TGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTTCGTTTCATCCAT  
AGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAA  
TGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAG  
CGCAGAAGTGGTCCCTGCAACTTTATCCGCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAG  
TAGTTCCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGT  
TTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAA  
AAAGCGGTTAGCTCCTTCGGTCCCTCCGATCGTTGTGTCAGAAGTAAGTTGGCCGAGTGTTATCACTCATGGT  
TATGGCAGCACTGCATAATCTCTTACTGTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACT  
CAACCAAGTCATTCTGAGAAATAGTGATGCGGCGACCGAGTTGCTCTTGCCCGCGTCAACACGGGATAAT  
ACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTTGAAAACGTTCTTCGGGGCGAAAACTCTCAAG  
GATCTTACCGCTGTTGAGATCCAGTTTCGATGTAACCCACTCGTGACCCAACTGATCTTCAGCATCTTTTA  
CTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAGGGAATAAGGGCGACA  
CGGAAATGTTGAATACTCATCTCTTCTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCAT  
GACATTAACCTATAAAAAATAGGCGT

FIG 12A

(1) C12ScFas Survival Construct

C12ScFas: epsilon-cFas (CD95)-Ires-Hygro-BGH PolyA put into C12s vector backwards so that no leaky transcription happens through the cmv promoter.

atcacgaggcccttctgcttcaagaacagctttgctcttaggagtttcttaatacatcccdadactcaaatatataaagc -40  
 atttgacttgttctatgcccagttatataatagtaataacacggggtcatttagttcatagcccataataggagttccg  
 cgttacataacttacggtaaatggcccgctgggtgaccgcccacgacccccgccattgacgtcaaatatgacgtatg  
 ttcccatagtaacgcaatagggaactttccattgacgtcaaatggggtgagttttacggtaaaactgcccacttggcagta  
 catcaagtgtatgccaagtacgccccctattgacgtcaatgacggtaaatggcccgctggcattatgccagta  
 catgaccttatgggactttctacttggcagtagatctacgtattagtcacgtattaccatgggtgatgcgggtttggc  
 agtacatcaatgggctggatagcgggtttagctcacggggtttccaaagtctccacccattgacgtcaatgggagtttg  
 ttttggcaccaaaatcaacgggactttccaaaatgtcgtaacaccccgcccatgacgtcaaatgggagtttaggcatgt  
 acgggtgggaggtctatataagcagagctcaataaaagagcccacaacccctcactcggggcgccagtcctccgattgact  
 gaggcgcccggttaccgtgtatccaaataaacctcttgcagttgcatcgcgacttgtggtctcgtgttcttgggaggg  
 tctctctgagtgattgactacccgtcagcggggtcttctcatttgggggtcgtcgggagtcgggagccctgcccag  
 ggaccaccgaccaccacgggaggttaagctggccagcaacttctctgtctgtcgtcgtgattgtctagtgtctatgactga  
 ttttatgctgtcgtacgtacgtactagttagctaaactagctctgtatctggcgaccggtggtggaactgacgagttcgga  
 caccggcgcaacccctgggagacgtcccagggaacttcggggcgcttttttggggccgacgtgagtcacaaaatcccga  
 tcgttttggactcttgggtgcaccccccttagaggagggatagtgtgttctggtaggagacgagaacacaaacagttcc  
 cgctcctcgctgaatttttgccttgcgttgggaggaacggcgccgctgtctgtctgctgagcatcgttctgtgt  
 tgtctctgtcgtgtgttctgtatttctgtatgtgaaaaatattgggcccgggagactgttaccactcccttaagtttgac  
 cttaggtcactggaaagatgtcgagcggatcgtctcaaacacagtcggttagatgtcaagaagagacgttgggttaccttct  
 gctctgcagaatggccaacctttaacgtcggatggcgcgagacggcacctttaaccgagacctatcacccctgcttaag  
 atcaaggtcttttaccctggccgcagtgacacccagcagcttccctacatcgtgacgtggaacccctggcttttga  
 cccccctcgctgggtcaagccctttgtacacccctaaagcctcgccctctcttctccatccgccccgtctctcccccttg  
 aacctcctcgttcgaccccgctcgtatcctccctttatccagccctcactcctctcttaggcgcccccatatggccat  
 gagatcttatatggggacccccgccccctgttaaaccttccctgacctgacatgacaagagttaactaacagccctctct  
 ccaagctcacttacaggtctcttacttagtcagcagaaacttctggagacctctggcgagccttaaccaagaacactgg  
 accgacgggtgggtacaccttaccaggtcggcgacacagtggtgggtcggcgacaccagactaagaacctagaacct  
 cgctggaaaggaccttaacagctcctgctgaccacccccacggccctcaaagttagacggcatcgagcttggatacacgc  
 cgccacgtgaaggctgcgcgaccccggggtggaccatcctctagactgcccGGATCTCGAGGGATCTCCCCAGCATGCC

TGCTATTGTCTTCCCAATCTCCCCCTTGCTGTCTGCCCCACCCACCCCCAGAAATAGAATGACACCTACTCAGACAA

TGCGATGCAATTTCTCTATTTATTAGGAAAGGACAGTGGGAGTGGCACCTTCCAGGGTCAAGGAAGGCACGGGGAGGG

GCAACAACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGtCTAGCTTGCCAAACCTACAGGTGGGGTCTTTTATTCCC

CCCTTTTTCTGGAGACTAAATAAAATCTTTTATTTTatcgatagatcccggtcggcatctactctattcctttgcctcgc  
 gacgagtgctggggcgctcggtttccactatcgccgagtagtcttctacacagccatcggtccagacggccgcgcttctgcgg  
 gcgatttgtgtacgcccagacagtcggggtcggatcgagcagattgctgctcagacccctgcgcccagctgcacatc  
 gaaattggcgtcaaccaagctctgtagagttggtcaagaccaatcgggagcatatacggccggagccgcgcgatctg  
 caagctccggatgcctccgctcgaagtagcgctgctgctcctacatacagccaaccacggccctccagaagaagattgt  
 gcgacctcgtattgggaatccccgaacatcgccctcgtcgcagacccctgttatgctggccattgtccgtcaggac  
 attgttggagccgaaaatccgctgcacgaggtgcgggacttcggggcagtcctcggccaaagcatcagctcatcgagag  
 cctgcggcagcggacgactgacggtgtcgtccatcacagtttgcagtgatcacatggggatcagcaatcgcgcatatg  
 aaatcacgccatgtagtgtattgacgattccttgcggtccgaattgggcccgaacccgctcgtctggctaaagatcgccgc  
 agcgatcgcatctatggcctcgcgacgggtcgagaaacagcgggcagttcggtttcaggcaggtcttgcaacgtgacac  
 cctgtgcaaggcgggagatgcaatagggtcaggctctcgctaaattccccaatgtcaagcacttcgggaatcgggagcgcg  
 gccgatgcaaatgcccataaacataacgatctttgtagaaccatcgggcgagctatttaccgcaggacatatccacg  
 cctcctacatcgaagctgaaagcagagattcttcgcccctcgagagctgcatcaggtcggagacgtgtcgaactttt  
 cgatcagaaacttctcgacagacgtcgcggtgagttcaggctttttcatgggtattatcatcgtgtttttcaaggaaaac  
 cagctccccgtggttcggggggcctagacgttttttaacctcgactaaacacatgtaagcatgtgcaccgagggccccag  
 atcagatcccatataatggggtaccttctgggcatccttcagcccttgttgaatagccttgaggagagccatttgactc  
 tttccacaactatccaactcacaacgtggcactgggggtgtgcccgccttgcaggtgtatcttatacacgtggcttttgg  
 ccgagaggcacctgtcgccaggtgggggttccgctgcctgcaaaaggtcgctacagacgtgttgtcttcaagaagc  
 ttCCAGAGGAAGTCTTCTTCTACGACATTCACAGACCTTGCAATCTTTGGCGAGAGGGGAAAGACCCctagactaga

ccaagctttggatttcatcttgaagtttgaattttctgagtcactagtaatgtccttgaggatgatagtcgaattttc  
 tctgcaagagtagaaaagattggcttttttgagatcttttaacatgtgtcatacgttcttttccatgaagttgatg  
 ccaattacgaagcagttgaactttctgttctgctgtgtcttggacattgtcatcttctgatctcatctattttggcttcat  
 tgacaccattctttcgacaaagcctttaacttgacttagtgcatgactccagcaatagtggtgatataatttactcaag  
 tcaacatcagataaatttattggcactgtttcaggatttaaggttggagattcatgagaaccttgggttttcttctgtg  
 ctttctgactgttttctgttcttctcaccacaaactatagtggaattggcaaaagaagaagacaaagccacc  
 ccaaccggtTTTCTGGGACTTTGTTTCTGTCAGTTTGTATTGCTGGTGTGTCATGGCTCAAGGGTTCATGTTTACAC

GAGGCGCAGCGAACACAGTGTTCACAGCCAGGAGAATCGCAGTAGAAGTCTGGTTTGCACCTGCACTTGGTATTCTGGGT

CAGGGTGCAGTTTGTCTTCCACTTCTAAACCATGCTCTTCATCGCAGAGTGTGCATCTTCTGCATTTATCAGCATAATGGT

TCTTGTCCATGTACTCCTTCCCTTCTGTGCATGGGGCACAGGTTGGTGTACCCCCATTCAATTTTGAGTCTCTCAACTTTT



aatagtgtatgcgggcgaccgagttgtctcttgcggcgctcaacacgggataataccgcgccacatagcagaactttaaa  
gtgtctcatcatggaaaacgttcttcggggcgaaaactctcaaggatcttaccgctgttgagatccagttcgatgtaacc  
cactcgtgcacccaactgatcttcagcatcttttactttaccagcgtttctgggtgagcaaaaacaggaaggcaaaatg  
ccgcaaaaaagggaataaggggcgacacggaaatgttgaaatactcatactcttcttttcaatattattgaagcatttat  
cagggttattgtctcatgacattaacctataaaaaataggcgt

[illegible]

FIG 13 A

(2) Ahhhh: Survival construct

2.) Ahhhh: epsilon-cFas' (CD8 or mLy2)-Ires-Hygro-BGHpolyA also in C12s backwards

atcacgaggcccttctgcttcaagaacagcttggctcttaggagtttqctaatacatercaaaactcaaptatataaage 60 80  
atttgacttgttctatgcccctagttattatagtaatacaattacggggtcatttagttcatagcccataatgaggttccg  
cgttacataacttacggtaaatggcccgctgggtgacggcccaacgacccccgccattgacgtcaataatgacgtatg  
ttcccatagtaacgccaatagggaactttccattgacgtcaatgggtggagtatttacggtaaaactgccacttggcagta  
catcaagtgtatcatatgccagtagtccccctattgacgtcaatgacggtaaatggcccgctggcatatgcccagta  
catgaccttatgggactttccctacttggcagtagatctacgtatttagtcatcgctattaccatgggtgatgagggttttgg  
agtagcatcaatggggtggatagcgggtttagctacgggggatttccaagtctccacccattgacgtcaatgggagttt  
ttttggcaccaaaatcaacgggactttccaaaatgtcgttaacaactccgccccattgacgcaaatggggttaggcattg  
acgggtgggaggtctataaagcagagctcaataaaagagcccaacccctcactcggggcgccagctcctccgattgact  
gagtcgccccgggtaccctgttatccaataaacctcttgcagttgcatccgacttgggtctcgctgttccctgggaggg  
tctcctctgagtgattgactaccgctcagcgggggtctttcatttgggggtcgtccgggagtcgggagacccctgccag  
ggaccacggacccaccacgggaggttaagctggccagcaacttatctgtgtctgtccgattgtctagtgtctatgactga  
ttttatgcccctgctgctgtagttagtctaactagctctgtatctggcgacccgtgggtggaactcggaaactcggaa  
caacggccgcaacccctgggagacgtccagggacttcggggggcgtttttgtggcccgacctgagtcacaaaaatccga  
tcgttttggactctttgggtgaccccccttagaggagggatattgtggttctggttaggagacgagaacctaaaacagttcc  
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tgtctctgtctgactgtgttctgtattgtctgaaatatggcgccggccagactgttaccactcccttaagttagttag  
cttaggtcactggaagatgtcagcggatcgctcacaaccagtcggtagatgtcaagaagagacgttgggttaccttct  
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atcaaggtcttttccactggcccgatggacacccagaccaggtccctacatcgtagctgggaagccttggcttttga  
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aacctcctcgttgcacccgctcgatcctccttataccagccctcactccttctctagggcggcccatatggccat  
gagatcttatatggggcaccctccgcccccttgtaaactccctgacccctgacatgacaagagtactaacagccccctct  
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cggtggaaaggaccttacacagtcctgctgaccacccccaccgcccccaagtagacggcatcgagcttggatacacgc  
cgccacgtgaaggctgcccacccccgggggtggaccatcctctagactgccGGATCTCGAGGGATCTCCCCAGCATGCC

TGCTATTGCTTCCCAATCCTCCCCCTTGCTGTCTGCCCCACCCACCCCCAGAATAGAATGACACCTACTCAGACAA

TGCGATGCAATTTCTCATTTTTATTAGGAAAGGACAGTGGGAGTGGCACCTTCCAGGGTCAAGGAAGGCACGGGGGAGGG

GCAACAACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGCTAGCTTGCCAAACCTACAGGTGGGGTCTTTCATTCC

CCCTTTTCTGGAGACTAAATAAAATCTTTTATTTTatcgatagatcccggtcggcatctactctattccttggccctcg  
gacgagtgctggggcgctcggtttccactatcgccgagtagtctctacacagccatcggtccagacggcgctctctcg  
gcatattgtgtacggcagacgtcccggtcggatcgagagattggtcgcacgacctcgcccaagctgcatcctc  
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caagctccggatgctccgctcgaagtagcgctctgctgctccatacaagccaaccacggcctccagaagaagatgttg  
gcgacctgctattgggaatccccgaacatcgctcctcgctccagtcattgaccgctgttatgcccattgtccgbcaggac  
attgttggagccgaatcccggtgacgaggtgcccgaacttcggggcagtcctcgcccaaaagcatcagctcatcgagag  
cctgcccagcggacgactgacggtgtgctccatcacagttagccagtgatacacatggggatcagcaatcgccgcatatg  
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cctgtgcacggcgaggatgcaataggtcaggtctcgtctaaattccccaatgtcaagcacttccggaatcgggagcg  
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ccctcctacatcgaaagctgaaagcacgagattcttcgcccccgagagctgcatcaggtcggagacgtgtcgaacttt  
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ttCCAGAGGAACCTGCTTCTTACGACATTCAACAGACCTTGCATTCTTGGCGAGAGGGGAAAGACCctagactaga

ccaagcttggatttcatcttgaagtttgaattttctgagtcactagtaatgtccttgaggatgatagcttgaattttc  
cttgaagagatacaagattggctttttttagatctttaaataatgtgtacacgttcttcttccatgaagttgatg  
ccaattacgaagcagttgaactttctgtctgtgtcttggacattgtcattctttagtctcatctattttggcttcat  
tgacaccattcttctgaacaaagcctttaacttgacttagtgcagtagtccagcaatagtggtgatattttactcaag - 33

F1- 13 B

tcaacatcagataaaatttattgactgtttcaggatttaaggttggagattcatgagactcttggttttcccttctgtg  
ctttctgcatgttttctgtacttcttctcttccaccaaacaattagtggaattggcaaaagaagaagacaaagccacc  
ccaaccgggtttccgggtcccttctactgagccacggggccgacaatcttctggtctctggtggtgagatgtcccggtaggg  
tgcacaggtgagggagttcgacagcactggcttggtagtagtagtgcacttctgaaggactggcagcagacagaactgaa  
gtacatcacccaggttggtagtagtgcagcagaaatagtagccttctgttcttctgctgaactgttcagggtgagaacgt  
acttattattctgtgtccctcatggcagaaaacagtttcgacgaattcagcttctctgctccacgttatcttgttgtgggat  
gaagccatatagacaacgaaggtggggtgggggagtttggagctggagtcttgggaagagccaagagcatccttgcgaaac  
ggaccccaacacttcacataccaggtccacacttctgaccaagtctggcggtccatttcttggaaagattcggagttctg  
gtgcctgtggcttagcttctccactccccaggataatcgactcaccagcagcagcaggttcagcgacagaaagcgggtc  
aacggtgaggccatgGTGGCTTTACCAACAGTACCGAATGCCAAGCTTGC GGCCGCTTAAGAGCTGTAATTGAACCTGG

GAGTGGACACCTGTGGAGAGAAAGGCAAAGTGGATGTCAGTAAGACCAATAGGTGCCTATCAGAAACGCAAGAGTCTTCT  
CTGTCTCGACAAGCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATACTTACCTGCCAGTGCCTCAGC

ACCAACTTctgcaggaattcctggacagctcccagatgatcagtaaccgtggtgttatttctgtgcccgggagtgagc  
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gttcccttttctctctgttcttgggaagtcgattgagcaacagcgggggtcaggtgaggtccttctactaccgatgcaca  
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cctctgcttccacgaaagccttgtgaagaaaggttggggcgcttcttgtgcaggagaatgaggcgactgaggtgaactg  
gcccccggggGcgctgttccagatgtgtgtgcagggcctcctgatggcgcagccctcgtccctgtgacccgcttggag  
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TCACTGACTCGCTGCGCTCGGTCTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACA

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GACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATAC - 85

CTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGT

TGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACATATCGTCTTGAGT

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CAGCGATCTGTCTATTTCTGTTTATCCATAGTTGCCGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCA - 74

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AAGGGCCGAGCGCAGAAGTGGTCTGCAACTTTATCCGCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAA

GTAGTTCCGCAGTTAATAGTTTGGCGAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTACGCTCGTCTTGGTATG

FIG 13C

GCTTCATT CAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTT 98  
CGGTCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTA  
CTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGagtactcaaccaagtcattctgagaatagtgatatgcggcga  
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agggcgacacggaaatgttgaatactcatactcttccttttcaatattattgaagcatttatcaggggtattgtctcat  
gacattaacctataaaaataggcgt

# Diphtheria toxin



Fig 14

Fig 15

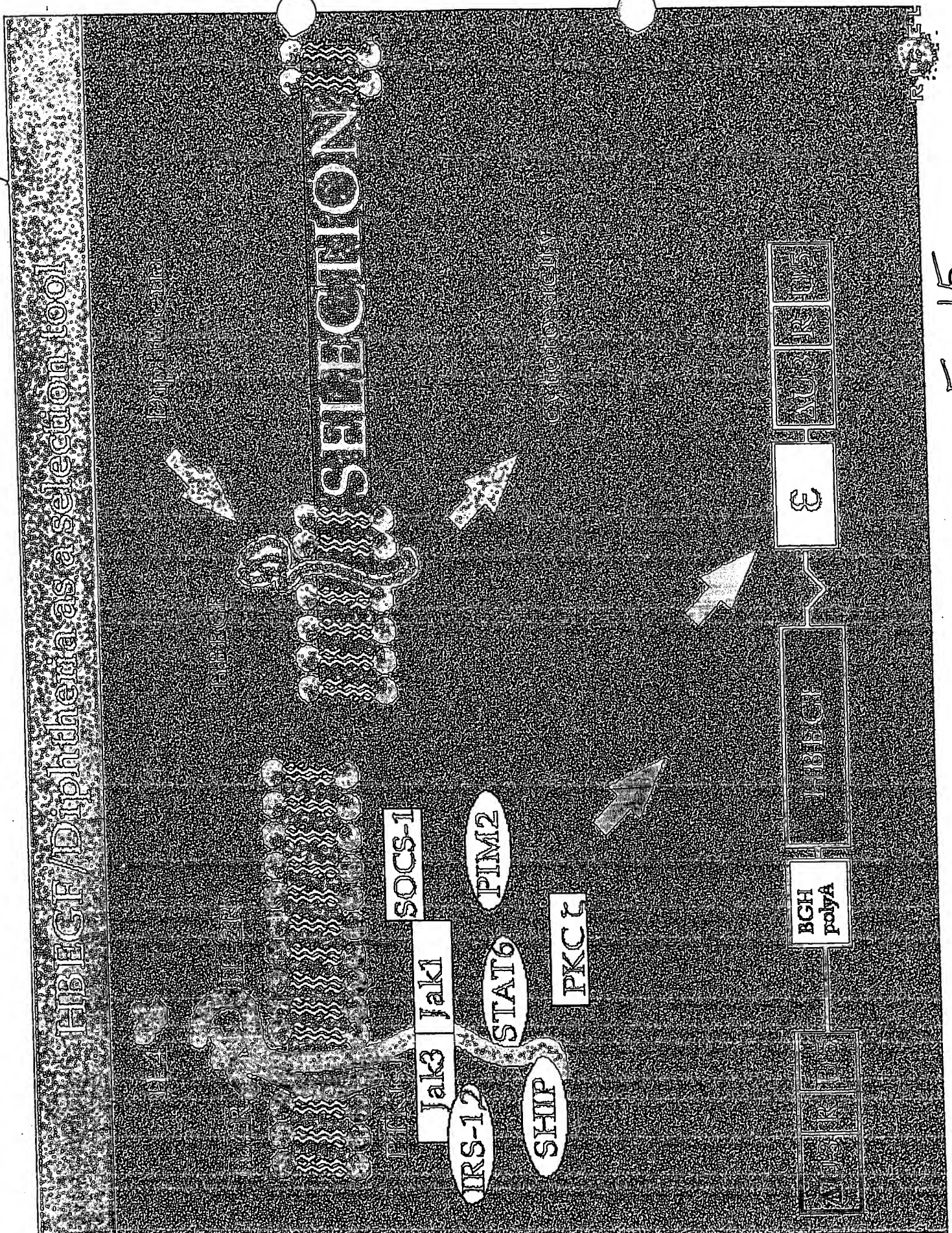
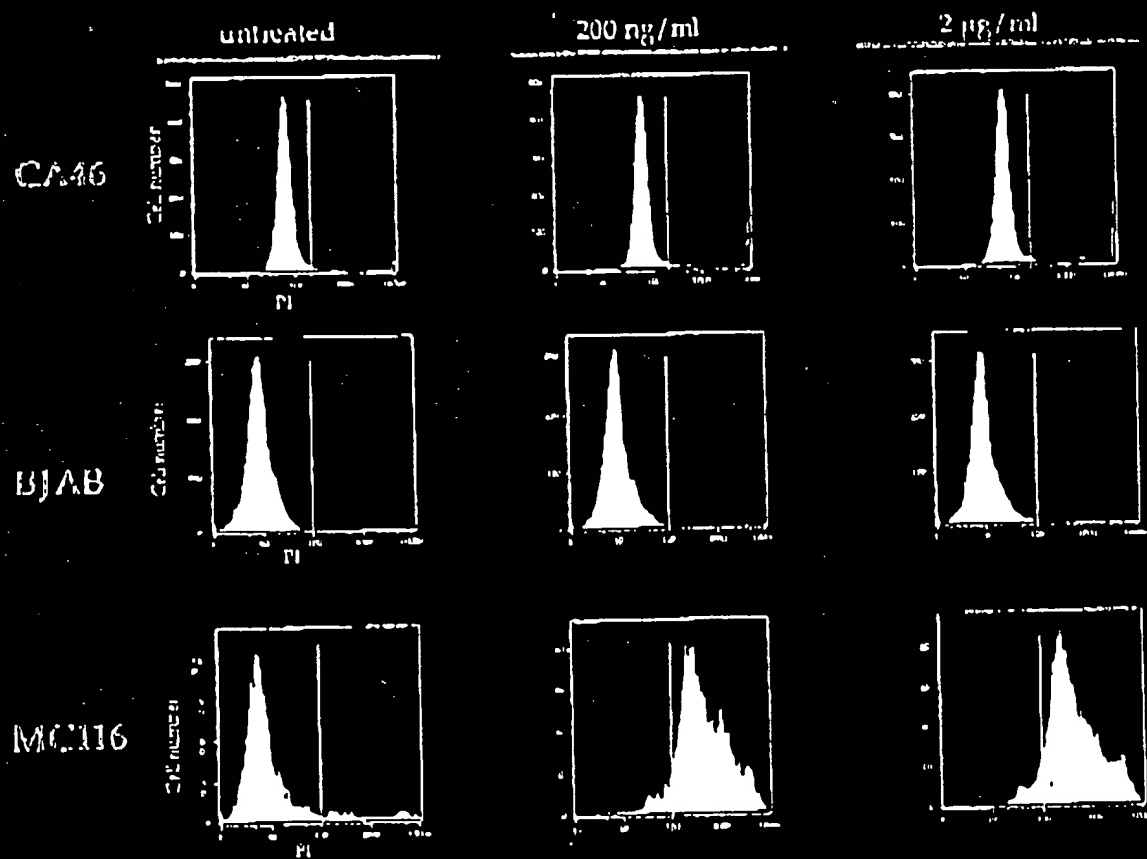


Fig 15

## 2nd generation selection systems

### Diphtheria sensitivity

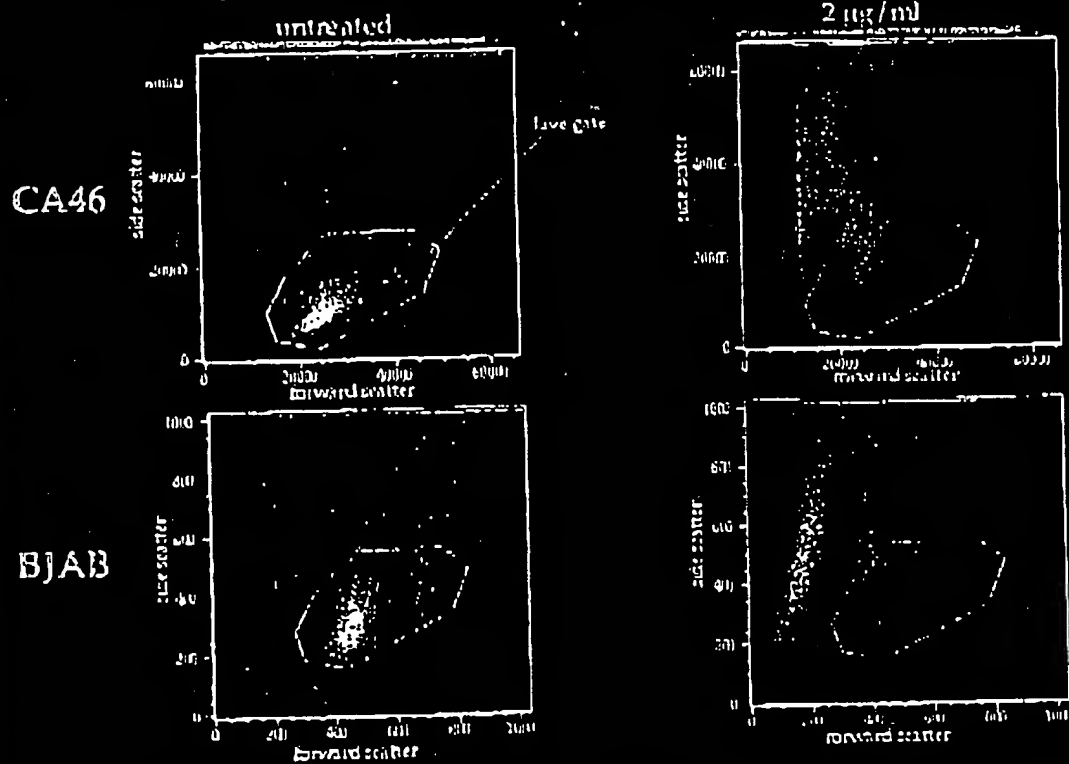


RIEEL

Fig 16

## 2nd generation selection systems

Ectopic expression of HBEGF confers diphtheria sensitivity



RIGEL

Fig 17

# Fig 18

